Brief report

Enrollment of underserved racial and ethnic populations in pediatric asthma clinical trials

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Background: The existing data on enrollment trends of historically underserved racial and ethnic children in clinical trials are limited.

Objective: We sought to evaluate documentation and representation of race and ethnicity in pediatric asthma clinical trials in the United States.

Methods: This is a cross-sectional study of United States–based interventional trials studying pediatric asthma that were completed between 2008 and 2022 and registered on ClinicalTrials.gov. Enrollment disparities were assessed by using the measure enrollment prevalence difference (EPD) (defined as the median difference between the proportion of participants enrolled and asthma prevalence in the US population by race and ethnicity).

Results: Of the 67 trials reviewed, 53 (79.2%) and 36 (53.7%) reported on race and ethnicity at ClinicalTrials.gov, respectively. Most participants were White (39.1%), Black (37.1%), or non-Hispanic (66.1%). Black, Hispanic, multiracial, and White children were enrolled in the expected proportions based on their contribution to asthma burden. However, American Indian or Alaska Native (AI/AN) (EPD = –1 [95% CI = –1 to –1]) and Asian children (EPD = –3 [95% CI = –3 to –3]) were underrepresented relative to disease burden in these respective groups. Fewer Black children were enrolled in drug or device trials (β = –0.80 [95% CI = –1.60 to –0.01]) than in other trials. Fewer Hispanic children were enrolled in early-phase than late-phase trials (β = –2.42 [95% CI = –3.66 to –1.19]).

Conclusions: Enrollment in pediatric asthma trials conducted in the United States was commensurate with the demographics of children affected by asthma for most racial and ethnic groups, but American Indian or Alaska Native and Asian children were underrepresented. Concerted efforts are needed to promote inclusion of these underserved groups in future trials. (J Allergy Clin Immunol Global 2024;3:100315.)

Key words: *Asthma, disparities, pediatric clinical trials*

INTRODUCTION

Prior studies of adult trials showed that historically marginalized racial and ethnic groups are underrepresented in clinical trials.[1-3] In pediatric trials, there are documented gaps in the reporting of race and ethnicity, although the data on documentation and enrollment trends in trials for specific pediatric conditions remain limited.[4-6] Representation of historically marginalized racial and ethnic children in pediatric trials is critically important to ensure generalizability of findings and promote equal access to state-of-the-art treatments. Equitable representation of race and ethnicity in asthma trials is particularly important given that asthma is the most common chronic childhood disease and the disease burden is disproportionately borne by historically marginalized racial and ethnic children.[7] Compared with non-Hispanic White children, Black and Hispanic children have higher rates of asthma prevalence, emergency department visits, hospitalizations, and mortality.[7]

We performed a cross-sectional review of United States–based interventional trials studying asthma in children (aged <18 years) that are registered on ClinicalTrials.gov. Our goal was to evaluate the documentation and representation of race and ethnicity in pediatric asthma clinical trials in the United States and identify trial characteristics associated with enrollment. This study received an exempt determination from the Boston Children's Hospital institutional review board.

RESULTS AND DISCUSSION

Between January 1, 2008, and December 31, 2022, a total of 67 United States–based interventional trials on pediatric asthma registered with results were available on ClinicalTrials.gov (Fig 1, and see Table E1 in this article's Online Repository at www.jaci-global.org). Of these trials, 53 (79.2%) provided information on race and 36 (53.7%) on ethnicity either through ClinicalTrials.gov or through available publications. Of those trials that reported race, 50 (94.3%) reported in ClinicalTrials.gov, and of the 36 that reported ethnicity, 33 (91.7%) reported in ClincialTrials.gov. In the trials reporting race, individuals classified as White, Black, multiracial, American Indian or Alaska Native (AI/AN), Asian, and Native Hawaiian or other Pacific Islander comprised 39.1%, 37.1%, 13.9%, 1.4%, 0.7%, and 0.3% of the study

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Abbreviations used
AI/AN: American Indian or Alaska Native
EPD: Enrollment prevalence difference
NIH: National Institutes of Health

participants, respectively (Table I). Of the participants in those trials that reported ethnicity, the majority (66.1%) were non-Hispanic. Table II summarizes the characteristics of these trials.

We assessed the representation of each race and ethnicity, relative to their contribution to pediatric asthma burden in the United States. We quantified enrollment prevalence disparity (EPD), which is defined as the median difference between the proportion of participants enrolled and pediatric asthma prevalence by race and ethnicity in the US population. A negative EPD signifies underrepresentation for a given racial or ethnic subgroup, whereas a positive EPD signifies overrepresentation (for detailed methods, see the Online Methods in the Online Repository at www.jaci-global.org). Our analysis showed that the enrollments of White (EPD = –6 [95% CI = –13 to 3]), Black (EPD = 8 [95% CI = –1 to 21]), Hispanic (EPD = 2 [95% CI = –14 to 9]), and multiracial children (EPD = –2 [95% CI = –5 to 2]) were commensurate with the prevalence of asthma in these respective populations. The majority of trials, however, underrepresented White children (60%) and overrpresented Black (60%) and Hispanic (53%) children. Enrollment of these groups varied widely across trials, as indicated by the wide CIs of their EPDs (Fig 2). AI/AN children (EPD = –1 [95% CI = –1 to –1]) and Asian children (EPD = –3 [95% CI = –3 to –3]) were significantly underrepresented relative to the disease burden in these respective groups across all trials. The year of trial commencement was not associated with enrollment of any racial and ethnic groups (see Table E2 in the Online Repository at www.jaci-global.org).

We developed regression models to evaluate the association between trial attributes and the proportion of participants enrolled in each trial by race and ethnicity. Table I summarizes the trial attributes assessed (for detailed methods, see the Online Methods). Our analyses showed that White children enrolled in treatment trials (β = 1.56 [95% CI = 0.52-2.61]) more often than in preventive or supportive trials. They were also more likely to enroll in drug or device trials (β = 1.57 [95% CI = 0.80-2.35]) than in trials with other (eg, behavioral) interventions (Fig 3). In contrast, a significantly lower proportion of Black children were enrolled in drug or device trials (β = –0.80 [95% CI = –1.60 to –0.01]) than in trials with other interventions. Hispanic children had lower enrollment in early-phase trials (β = –2.42 [95% CI = –3.66 to –1.19]) than in late-phase trials and higher enrollment in federally funded trials (β = 1.96 [95% CI = 0.15-3.76]) than in trials without federal funding.

Our study highlights the need to improve reporting of race and ethnicity in pediatric clinical trials. Consistent with the findings of Rees et al, only half of the trials reviewed reported on ethnicity. In contrast, Lee et al demonstrated that most trials funded by the National Institutes of Health (NIH) reported race (94%) and ethnicity (78%) of enrollees.[4,5] The higher rates of reporting among trials funded by the NIH may reflect NIH reporting requirements published within the past decade,[8] reinforcing the importance of mandating reporting of race and ethnicity in clinical research.

Consistent with Rees et al, we found that Asian and AI/AN children were underrepresented in United States–based pediatric trials.[5] Rees et al further showed that enrollment of Hispanic children in United States–based pediatric trials was representative of the US population, whereas Black children were enrolled at a rate 88% higher than expected.[5] In comparison, a study by Lee et al demonstrated overrepresentation of AI/AN, Asian, Black, Latino, and Native Hawaiian or Pacific Islander children in NIH-funded pediatric clinical trials.[4] A number of factors may explain these differences. First, whereas these studies examined pediatric trials in general, our study focused on asthma and trial enrollment may vary by diseases. Second, whereas we compared enrollment by race and ethnicity with respect to asthma prevalence in these groups, both Rees et al[5] and Lee et al[4] assessed representativeness of trial enrollment relative to the US population. The latter approach does not account for the burden of disease, which may vary across different racial and ethnic groups, as is the case for asthma. Nonetheless, the findings that Black and Hispanic children were represented in pediatric asthma trials in proportions relative to their disease burden are encouraging, given that these groups are often underrepresented in research. International trials often enroll children of European origin at proportions higher than the proportions of Black and Hispanic children, such that the demographic makeup of trial participants is not reflective of the US population of children with asthma.[9,10] The findings here suggest that the important work being done in the United States to address these disparities has facilitated enrollment of underserved children in clinical trials.[11,12] In particular, sponsored directives, such as the Inner City Asthma Consortium within the National Institute of Allergy and Infectious Diseases, which focus on enrollment of children with asthma living in urban environments, have been integral to the enrollment of a diverse population of children in asthma trials.[13]

The underrepresentation of AI/AN and Asian children in asthma trials is concerning, however. AI/AN children are twice as likely as White children to have asthma.[7] Moreover, the overall death rates for AI/AN children with asthma are 41% higher than those for White children in the United States.[14] Among Asian Americans, asthma prevalence varies widely by ethnic subgroups, with rates as high as 16% in Filipino Asian children.[15,16] The underrepresentation of AI/AN individuals in clinical research has been documented in other clinical domains.[17,18] A review of clinical studies conducted by the intramural research program of the NIH showed that AI/AN participants comprise only 1% of all participants, which is a disproportionately low level compared with the proportion of AI/AN individuals in the US population, which stands at 3%.[17] Cultural and historical issues may play a significant role in the recruitment of AI/AN individuals into clinical trials.[19] Furthermore, the majority of AI/AN communities are located in rural areas. Poor access to health care, underfunded tribal health systems, geographic distance from research institutions, and socioeconomic factors are major barriers to trial participation among AI/AN communities.[20] Few studies to date have explored the causes underlying underrepresentation of Asian children in clinical trials. Given that this population has been shown to be consistently underrepresented in pediatric trials, further research is needed to understand and address barriers to trial participation among Asian children.

We further observed higher enrollment of White children in drug and device trials and lower enrollment of Black children in these trials. Historically, few interventional trials of drugs and

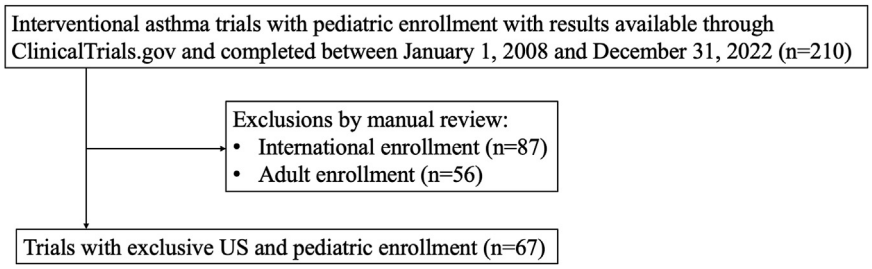

FIG 1. Flow diagram for selection of study trials

TABLE I. Distribution of race and ethnicity among participants in pediatric asthma clinical trials

Race and ethnicity	no. (%)
Race (n = 53 trials)*	
AI/AN	137 (1.4)
Asian	68 (0.7)
Black	3500 (37.1)
Native Hawaiian or Pacific Islander	30 (0.3)
White	3692 (39.1)
Multiple†	1331 (13.9)
Unknown	478 (5.1)
Ethnicity (n = 36 trials)	
Hispanic	2550 (30.9)
Non-Hispanic	5459 (66.1)
Unknown	149 (1.8)

*Percentage of each racial and ethnic group, as determined by number of patients in a given group divided by the total of patients across all trials that reported race (n = 9452) or ethnicity (n = 8263). Race and ethnicity are reported according to the National Institute of Health Office of Management and Budget standards.
†Multiple race has been defined as multiracial or other.

TABLE II. Characteristics of pediatric asthma clinical trials (n = 67)

Study design characteristic	no. (%)
Intervention purpose, no. (%)	
Prevention	5 (7.5)
Supportive	13 (19.4)
Treatment	49 (73.1)
Intervention type, no. (%)	
Drug/device intervention	50 (74.6)
Others (eg, behavioral)	17 (25.4)
Early-phase (phase 1 or 2 trial), no. (%)	16 (39.0)
Any blinding, no. (%)	38 (56.7)
Primary study site, no. (%)	
Nonprofit institution	55 (82.1)
Funding source, no. (%)	
Any government funding	22 (32.8)
Any industry funding	16 (23.9)
Enrollment and follow-up	
Multicenter enrollment, no. (%)	31 (46.2)
School-based enrollment, no. (%)	9 (13.4)
Total participants, median (IQR)	84 (29-245)
Follow-up frequency, median (IQR)	1 (1-2)
Follow-up duration (d), median (IQR)	112 (14-336)

IQR, Interquartile range.

devices for a variety of diagnoses and conditions have been conducted at institutions that primarily serve historically marginalized racial and ethnic children, which may have accounted for this observed difference.[21] We further observed lower enrollment of Hispanic children in early-phase trials. Prior studies have similarly documented racial and ethnic disparities in early-phase trial enrollment for other diseases.[22] Distrust of the medical system and fear and uncertainty of trial treatment were cited as barriers.[23] Language barriers further complicate patient-provider communications, trial recruitment, and patient eligibility.[23] Early-phase trials are designed to establish safety and dosing and involve the greatest uncertainty around potential efficacy. These trials, however, provide access to new investigational treatments that may be otherwise unavailable. Therefore, addressing barriers to participation in early-phase trials is needed to ensure equal access to state-of-the-art treatments.

Researchers in the fields of asthma, allergy, and immunology have identified participant inclusivity in clinical trials as a key strategy to advance health equity within the field. Future investigators may incorporate the findings of this work to achieve this stated goal within the context of asthma clinical trials. Proactive consideration of participant race and ethnicity at time of study design is needed.[24] For example, investigators may consider identifying criteria for enrollment by race and ethnicity at study onset based on contribution to underlying disease prevalence.[24] In addition, investigators may identify study sites based on enrollment capabilities. For trials in which interventions have already been rigorously tested within a homogenous population, additional study within a more diverse population of children may improve the generalizability of the work. Finally, given the known heterogeneity of asthma prevalence and morbidity within census-defined racial and ethnic subgroups, investigators should consider disaggregation of standard census-defined race and ethnicity categories into further subgroups and ensure that participant race and ethnicity are defined through self-report.[25]

Our analyses are limited by the availability and completeness of data captured on ClinicalTrials.gov and in available publications. There were 851 children (9.0% of the cohort) of either "other" or "unknown race" whom we were not able to capture in our EPD analysis. Missing race and ethnicity data may have skewed our analyses. To assess the impact of missing data, we conducted a sensitivity analysis excluding trials with missing race and ethnicity data in more than 25% of cases (n = 3); we did not observe significant changes in the resulting EPD (see Table E3 in the Online Repository at www.jaci-global.org). We further assessed whether the attributes of trials that did not report race and ethnicity differed from those that did, and our analysis did not show differences between these trials (see Table E4 in the Online Repository at www.jaci-global.org).

Our study highlights encouraging results with respect to enrollment of Black and Hispanic children in US pediatric asthma

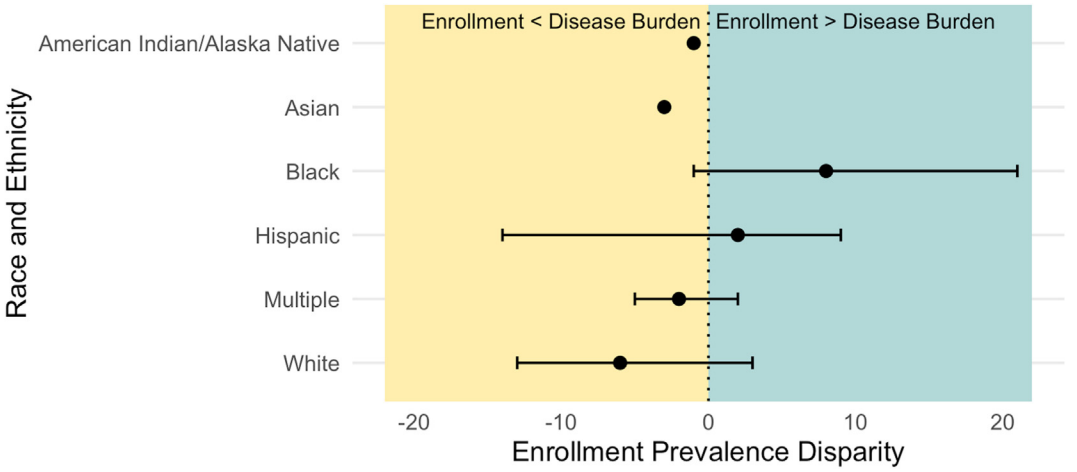

FIG 2. Median (95% CI) EPD by race and ethnicity. A wider CI indicates that trial enrollment varied widely. A narrow CI indicates that a group was consistently underrepresented or overrepresented in all trials. Native Hawaiian or Pacific Islander children were excluded from analysis, as we were not able to find reliable data for US pediatric asthma prevalence.

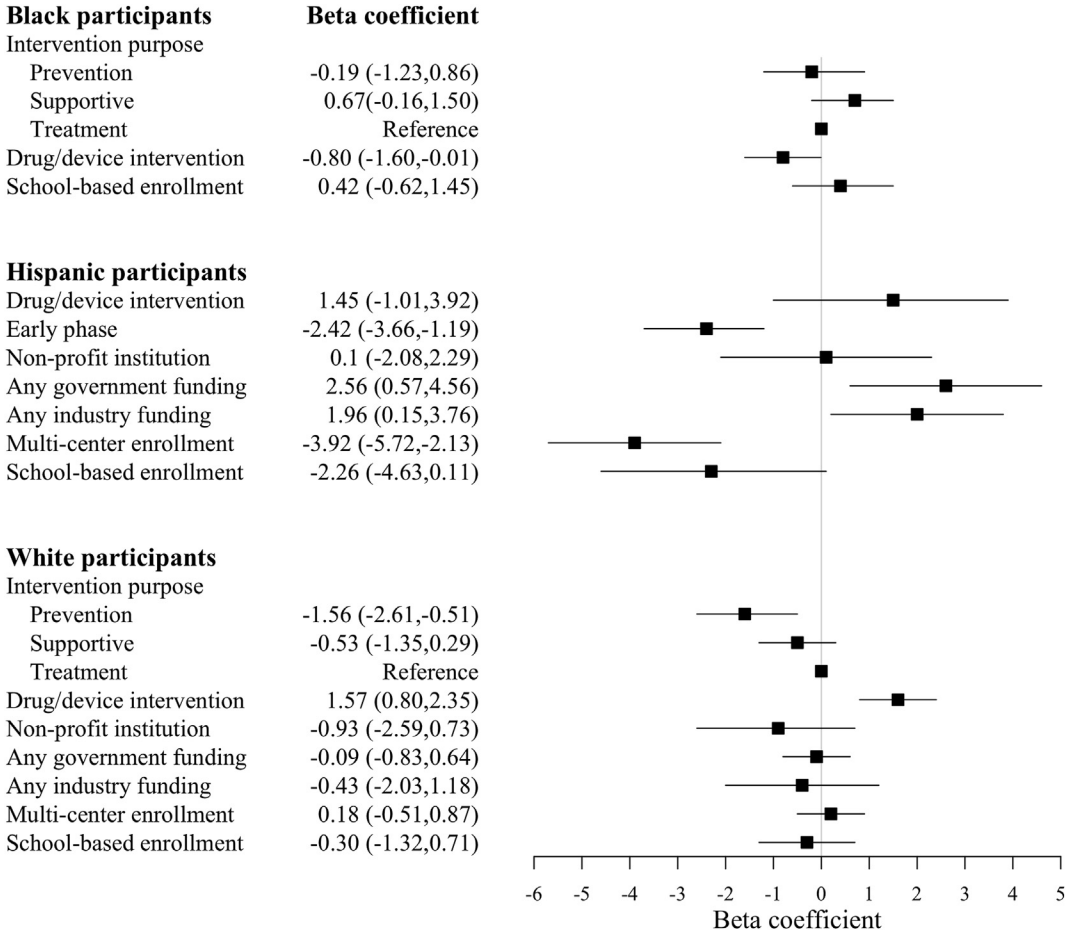

FIG 3. Multivariate analyses of trial attributes associated with enrollment for a givenracial and ethnic group. The analyses included only attributes that attained at values of *P* less than .2 in univariate analyses (see Table E2).

clinical trials, while also demonstrating the need for improved enrollment of AI/AN and Asian children and universal reporting of participant race and ethnicity in clinical trials. Strategies for promoting recruitment of these underrepresented populations are needed to ensure equitable inclusion of all racial and ethnic groups in pediatric asthma trials.

DISCLOSURE STATEMENT

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Key messages

- **Enrollment in pediatric asthma trials conducted in the United States was commensurate with the demographics of children affected by asthma for most racial and ethnic groups; however, American Indian and Alaska Native and Asian children were underrepresented relative to their contribution to asthma burden.**
- **Strategies for promoting recruitment of these underrepresented populations are needed to ensure equitable inclusion of all racial and ethnic groups in pediatric asthma trials.**

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